REMARKS

Reconsideration is requested.

Claims 63-70 are pending.

Reconsideration and withdrawal of the restriction requirement are again requested. A Rule 181 Petition requesting the same is attached with the requisite fee. Consideration of the attached Petition prior to issuance of a further Action on the merits is requested. Attached is a copy of a Decision issued in the parent application Serial No. 08/836,075, wherein the restriction requirement of the parent application was withdrawn by Decision of the Commissioner based on the previous allowance of the claimed subject matter. Similar considerations are relevant in the present application. Consideration of the attached, withdrawal of the restriction requirement and examination of all the claimed subject matter are requested.

The specification has been amended to include a cross-reference to the prior applications, as required by the Examiner on page 3 of the Office Action dated March 11, 2002 (Paper No. 11).

A copy of the Declaration in the Patent Office copy of the parent Serial No. 08/836,075 has been requested as a possible "clearer" copy of the Declaration. The same will be submitted by the undersigned once received from the Patent Office. The applicants would certainly appreciate the Examiner obtaining a clearer copy of the Declaration from the Patent Office copy of the parent file. The applicants note that the

full name of the first inventor is Geert Maertens, as noted in the Patent Office Filing Receipt.

The Section 101 rejection of claim 69 is traversed. Reconsideration and withdrawal of the rejection are requested as the Examiner's characterization of the claimed subject matter as a "polynucleic acid molecule" is not correct. In fact, claim 69 provides a host cell which has been transformed with the recited recombinant vector. The claimed host cell is submitted to define patentable subject matter. Withdrawal of the Section 101 rejection of claim 69 is requested.

The Section 112, second paragraph, rejection of claim 63 stated in paragraph 14 of Paper No. 11 is obviated by the above amendments. The applicants note however that the Patent Office had previously allowed claim 2, for example, of U.S. Patent No. 6,180,768 (copy attached) wherein the term "having" was not objected-to. The term is not indefinite however the claims have been amended to recite a more traditional term.

The Section 112, second paragraph, rejection of claim 63 in paragraph 15 of Paper No. 11 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the Patent Office previous allowance of, for example, claim 2 of U.S. Patent No. 6,180,768. The Examiner has not indicated or explained how the art, for example, has changed since the previous issuance of claim 2 of U.S. Patent No. 6,180,768, in a manner which would make one of ordinary skill question the metes and bounds of the objected-to phrase. Withdrawal of the Section 112, second paragraph, rejection of claims 63, 68 and 69 is requested.

Formal drawings are attached. Acceptance of the same in the Examiner's next Action is requested.

Grant of the attached Petition, prior to issuance of a further Action on the merits, is requested along with a Notice of Allowance relating to all the pending claims.

Respectfully submitted,

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US006180768B1

(12) **United States Patent**
Maertens et al.

(10) **Patent No.: US 6,180,768 B1**
(45) **Date of Patent: Jan. 30, 2001**

(54) **SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS PROPHYLACTIC, THERAPEUTIC AND DIAGNOSTIC AGENTS**

(75) Inventors: **Geert Maertens**, Bruges; **Lieven Stuyver**, Herzele, both of (BE)

(73) Assignee: **Innogenetics N.V.**, Ghent (BE)

(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

(21) Appl. No.: **08/836,075**

(22) PCT Filed: **Oct. 23, 1995**

(86) PCT No.: **PCT/EP95/04155**

§ 371 Date: **Apr. 21, 1997**

§ 102(e) Date: **Apr. 21, 1997**

(87) PCT Pub. No.: **WO96/13590**

PCT Pub. Date: **May 9, 1996**

(30) **Foreign Application Priority Data**

Oct. 21, 1994 (EP) 94870166
Jun. 28, 1995 (EP) 95870076

(51) **Int. Cl.**[7] C07H 21/04; C12Q 1/70; G01N 33/53; C12P 21/00

(52) **U.S. Cl.** 536/23.1; 536/23.72; 536/24.3; 435/5; 435/7.1; 435/69.3; 435/252.3; 435/320.1; 530/300; 530/350

(58) **Field of Search** 435/5, 7.1, 320.1, 435/69.3, 252.3; 530/300, 350; 536/23.1, 23.72, 24.3

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(57) **ABSTRACT**

The present invention relates to new genomic nucleotide sequences and amino acid sequences corresponding to the coding region of these genomes. The invention relates to new HCV types and subtypes sequences which are different from the known HCV types and subtypes sequences. More particularly, the present invention relates to new HCV type 7 sequences, new HCV type 9 sequences, new HCV type 10 and new HCV type 11 sequences. Also, the present invention relates to new HCV type 1 sequences of subtypes 1*d*, 1*e*, 1*f* and 1*g*; new HCV type 2 sequences of subtypes 2*e*, 2*f*, 2*g*, 2*h*, 2*i*, 2*k* and 2*l*; new HCV type 3 sequences of subtype 3*g*, new HCV type 4 sequences of subtypes 4*k*, 4*l* and 4*m*; a process for preparing them, and their use for diagnosis, prophylaxis and therapy. More particularly, the present invention provides new type-specific sequences of the Core, the E1 and NS5 regions of new HCV types 7, 9, 10 and 11, as well as of new variants (subtypes) of HCV types 1, 2, 3 and 4. These new HCV sequences are useful to diagnose the presence of HCV type 1, and/or type 2, and/or type 3, and/or type 4, and/or type 7, and/or type 9, and/or type 10, and/or type 11 genotypes or serotypes in a biological sample. Moreover, the availability of these new type-specific sequences can increase the overall sensitivity of HCV detection and should also prove to be useful for prophylactic and therapeutic purposes.

12 Claims, 74 Drawing Sheets

-continued

(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

Arg Pro Lys Tyr His Gln Val Thr Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO: 205:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

Arg Pro Arg Met His Gln Val Val Gln Glu
1 5 10

(2) INFORMATION FOR SEQ ID NO: 206:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

Arg Pro Arg Met Tyr Glu Ile Ala Gln Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO: 207:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

Arg His Arg Gln His Trp Thr Val Gln Asp
1 5 10

We claim:

1. A Hepatitis C virus polynucleic acid, having a nucleotide sequence which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1; or the complement thereof.

2. A polynucleic acid which is chosen from the group consisting of

(i) the nucleotide sequences having SEQ ID 1, 3, 5, 7, 9, 11, 13 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103 or 105,

(ii) a part of said polynucleic acid of (i) which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1, and

(iii) the complement of the polynucleic acid of (i) or (ii).

3. A polynucleic acid according to claim 1, wherein the polynucleic acid is selected from

(i) a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequence at least one of the following amino acid residues: I15, C38, V44, A49, Q43, P49, Q55, A58, S60 or D60, E68 or V68, H70, A71 or Q71 or N71, D72, H81, H101, D106, S110, L130, I134, E135, L140, S148, T150 or E150, Q153, F155, D157, G160, E165, I169, F181, L186, T190, T192 or I192 or H192, I193, A195, S196, R197 or N197 or K197, Q199 or D199 or H199 or N199, F200 or T200, A208, I213, M216 or S216, N217 or S217 or G217 or K217, T218, I219, A222, Y223, L230, W231 or L231, S232 or H232 or A232, Q233, E235 or L235, F236 or G236, F237, I240 or M240, A242, N244, N249, I250 or K250 or R250, A252 or C252, A254,

I255 or V255, D256 or M256, E257, E260 or K260, R261, V268, S272 or R272, I285, G290 or F290, A291, A293 or L293 or W293, T294 or A294, S295 or H295, K296 or S296, Y297 or M297, I299 or Y299, I300, S301, P316, S2646, A2648, G2649, A2650, V2652, Q2653, H2656 or L2656, F2659, K2663 or I2663, A2667 or V1667, D2677, L2681, M2686 or Q2686 or E2686, A2692 or K2692, H2697, I2707, L2708 or Y2708, A2709, A2719 or M2719, F2727, T2728 or D2728, E2729, F2730 or T2730, I2745, V2746 or E2746 or L2746 or K2746, A2748, S2749 or P2749, R2750, E2751, D2752 or N2752 or S2752 or T2752 or V2752 or I2752 or Q2752, S2753 or D2753 or G2753, D2754, A2755, L2756 or Q2756, R2757, with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering as shown in Table 1.

(ii) a part of said polynucleic acid of (i) which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1.

(iii) or the complement of the polynucleic acid of (i) or (ii).

4. A polynucleic acid according to claim 1, wherein the polynucleic acid is selected from

(i) a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequences at least one amino acid sequence chosen from the group consisting of the amino acid sequences having SEQ ID 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104 or 106.

(ii) a part of said polynucleic acid of (i) which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1.

(iii) or the complement of the polynucleic acid of (i) or (ii).

5. A polynucleic acid according to claim 1, wherein the polynucleic acid is selected from

(i) a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequence at least one amino acid sequence chosen from the group consisting of the amino acid sequences having SEQ ID 107 to 207,

(ii) a part of said polynucleic acid of (i) which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1.

(iii) or the complement of the polynucleic acid of (ii) or (iii).

6. A polynucleic acid according to any of claims 1 to 5 which comprises 5' UR sequences, the Core/E1 and the NS4 or the NS5B region or a part thereof.

7. A recombinant polypeptide encoded by a polynucleic acid according to any of claims 1 to 5 or a part thereof which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1.

8. A method for production of a recombinant polypeptide, comprising:

transformation of an appropriate cellular host with a recombinant vector, in which a polynucleic acid or a part thereof according to any of claims 1 to 5 has been inserted under the control of the appropriate regulatory elements, the polynucleic acid or the part thereof thus being an insert,

culturing said transformed cellular host under conditions enabling the expression of said insert, and

harvesting said polypeptide

9. A recombinant expression vector comprising a polynucleic acid or a part thereof according to any of claims 1 to 5 operably linked to prokaryotic, eukaryotic or viral transcription and translation control elements.

10. A host cell transformed with a recombinant vector according to claim 9.

11. A peptide corresponding to an amino acid sequence encoded by one of the polynucleic acids according to any of claims 1 to 5, with said peptide comprising an epitope which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1.

12. The polynucleic acid of claim 1, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO:1.

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MAR 19 2003

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In re Application of	:	
Geert Maertens et al	:	
Serial No.: 08/836,075	:	PETITION DECISION
Filed: April 21, 1997	:	
Attorney Docket No.: 2752-31	:	

This is a decision on the petition under 37 CFR 1.181, filed December 19, 2002, requesting removal of an improper restriction requirement.

BACKGROUND

A review of the pertinent portion of the file history shows that this application was allowed and the Issue Fee was paid prior to September, 1999. Through error the application was held abandoned in August, 2000, and the abandonment rescinded in December, 2000. In January, 2001, a petition under 37 CFR 1.313 accompanied by an RCE request and an IDS statement was filed. The petition was granted on January 26, 2001, which was too late to prevent publication of the patent, per se. By Notice in the Official Gazette indication was given that no patent had issued for the assigned number. The application was then returned to the examiner for further action.

Subsequently several additional IDS statements were submitted as well as an amendment. The examiner mailed an Office action to applicants on November 19, 2002, setting forth a two way restriction requirement, as follows:

> Group I, claims 75-84, drawn to unique polypeptides from differing HCV genomes;
> Group II, claim 85, drawn to a purified polypeptide.

In addition, the election of a single amino acid sequence was required irrespective of whichever group was elected. Applicants replied on December 19, 2002, electing Group I and SEQ ID NO. 43 with traverse. Applicants also filed this petition to have the restriction requirement withdrawn.

DISCUSSION

Applicants argue that all of the claims currently active in the application were prosecuted and allowed by the same examiner in June, 1999. Applicants have amended the claims only to cancel one dependent claim and to remove some of the sequence identifiers from the claims so as to avoid newly submitted prior art. Applicants argue that since all of the claims were previously considered together they should not be divided now. Applicants basically argue that the Office has been inconsistent in prosecution of this application and that the restriction requirement should be withdrawn.

It is also noted that this application is the National Phase filing of PCT/EP95/04155. As such the making of a restriction requirement solely under 35 U.S.C. 121 without consideration of PCT Rule 13 provisions is improper. As only RCE papers have been filed this application remains a National Phase application.

DECISION

Applicants' petition is **GRANTED.**

The restriction requirement of the last Office action is withdrawn. The application will be forwarded to the examiner for consideration of the response filed December 19, 2002.

Should there be any questions with respect to this decision, please contact William R. Dixon, Jr., by mail addressed to: Director, Technology Center 1600, Washington, D.C. 20231, or by telephone at (703)308-3824 or by facsimile transmission at (703) 305-7230.

John Doll
Director, Technology Center 1600